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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/756,761	01/14/2004	Laurence S. Harbig	604-706	1504
23117 7590 03/16/2009 NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203				
EXAMINER				
KANTAMNINI, SHOUBHA				
ART UNIT		PAPER NUMBER		
1617				
MAIL DATE		DELIVERY MODE		
03/16/2009		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/756,761

Applicant(s)

HARBIGE ET AL

Examiner

Shobha Kantamneni

Art Unit

1617

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-11, 14 and 15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) NONE is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-11, 14-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/20/2009 has been entered.

Applicant's amendment received on 01/02/2009, wherein claim 1 has been amended.

Applicant's amendment overcomes the rejection of claims 1-3, 8-11, 13-15 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicant's amendment overcomes the rejection of claims 1-3, 6-9, 11, and 15 under 35 U.S.C. 102(b) as being anticipated by Lunardi et al. (Neurology, volume 48(6), 1997, pages 1714-1717, PTO- 892).

Upon, further consideration the rejection of claims 1-3, 6-9, 11, and 13 under 35 U.S.C. 102(b) as being anticipated by Bountra et al. (WO 00/61231, PTO-1449) is herein withdrawn.

Claims 1-3, 6-11, and 14-15 are examined herein, insofar as they read on the elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites the limitation "100 mg/day" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 6-9, 11 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bountra et al. (WO 00/61231, PTO-1449).

Bountra et al. discloses a method of treating multiple sclerosis comprising administering sodium channel antagonists which includes 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine. See page 7, lines 20-24; page 8, lines 5-10; page 14, claim 7. A dose range of sodium channel antagonist is 200 mg/day to 900 mg/day for an adult human. See page 10, lines 1-8. Bountra et al. also teaches that it may be necessary to make routine

variation to the dosage, depending on the age and condition of the patient. See page 10, lines 1-8.

Bountra et al. does not explicitly teach administration of lamotrigine in the method of treating multiple sclerosis i.e does not provide an example.

It would have been obvious to a person of ordinary skill in the art at the time of invention to administer lamotrigine to treat multiple sclerosis because Bountra et al. teach that sodium channel antagonist such as lamotrigine are useful in treating multiple sclerosis. Accordingly, one of ordinary skill in the art would have been motivated to administer lamotrigine with reasonable expectation of success of treating multiple sclerosis.

Further, regarding the recitations, "wherein the therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue", "wherein the therapy stabilizes the patients Expanded Disability Status Score, thus halting progress of the disease", in claims 8-9, since Bountra et al. render the claimed method of administration of effective amounts of lamotrigine for treating multiple sclerosis obvious, administration of lamotrigine necessarily results in reduction of one or more of incidence of relapse, spasticity and fatigue", halts progress of the disease, as claimed herein.

Response to Arguments

Applicant argues that "Bountra likewise contains no disclosure of the invention as claimed. Bountra proposes that sodium channel antagonists may be used to treat neuronal apoptosis. This is irrelevant to multiple sclerosis (MS), as it is well evidenced in the art that this mechanism is not significant in that disease." These arguments, and

the papers cited by the applicant have been considered, but not found persuasive. Bountra et al. clearly discloses that sodium channel antagonists are used for treating multiple sclerosis. See page 14, claim 7 of Bountra et al.; page 7, lines 20-24; page 8, lines 5-10.

Claims 10, 14-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bountra et al. (WO 00/61231, PTO-1449) as applied to claims 1-3, 6-9, 11.

Bountra et al. is applied as discussed above.

Bountra et al. discloses a method of treating multiple sclerosis comprising administering sodium channel antagonists such as 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine. See page 7, lines 20-24; page 8, lines 5-10. A dose range of 200 mg/day to 900 mg/day for an adult human is disclosed. Bountra et al. also teaches that it may be necessary to make routine variation to the dosage, depending on the age and condition of the patient. See page 10, lines 1-8.

Bountra et al. does not specifically teach the amount of lamotrigine as 600 mg/day as in claim 14, and the dosing regimen as in claim 15.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of lamotrigine to be administered in the method of treating multiple sclerosis.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of lamotrigine employed in the

method of treating multiple sclerosis, since the optimization of effective amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of known ingredients in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in the art.

Response to Arguments

Applicant argues that "Bountra provides no credible guidance on how to dose and what to dose. A person of ordinary skill in the art might easily have selected carbamazepine, as did Ramsaransing et al, and then dose at 900mg with serious detrimental effect." These arguments have been considered, but not found persuasive. Bountra et al. clearly discloses the use of a sodium channel antagonists such as 3,5-diamino-6-(2,3-dichlorophenyl)-1,2,4-triazine called lamotrigine, 5-amino-6-[2,3,5-trichlorophenyl]-1,2,4-triazine for the treatment of multiple sclerosis. See page 7, lines 20-24; page 8, lines 5-10. Bountra et al. teaches that the sodium channel antagonists therein are employed in dose range of 200 mg/day to 900 mg/day for an adult human, and it may be necessary to make routine variation to the dosage, depending on the age

and condition of the patient. One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in the art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 6-9, 11, and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lunardi et al. (Neurology, volume 48(6), 1997, pages 1714-1717, PTO-892).

Lunardi et al. discloses administration of lamotrigine to patients suffering from multiple sclerosis in which trigeminal neuralgia was also present. See abstract; page 1715. Lamotrigine was administered at an initial dosage of 25 mg/day, increasing in increments of 25 mg every third day up to a maximum absolute dosage of 400 mg/day. See page 1716, left hand column. Administration of lamotrigine to patients suffering from multiple sclerosis concomitant with trigeminal neuralgia resulted in complete pain relief.

Lunardi et al. does not specifically teach the specific amount of lamotrigine as between 500 mg/day and 700 mg/day.

It would have been obvious to a person of ordinary skill in the art at the time of invention to determine or optimize parameters such as effective amounts of lamotrigine to be administered in the method of treating multiple sclerosis.

One having ordinary skill in the art at the time the invention was made would have been motivated to determine the effective amounts of lamotrigine employed in the method of treating multiple sclerosis, since the optimization of effective amounts of known agents to be administered, is considered well in the competence level of an ordinary skilled artisan in pharmaceutical science, involving merely routine skill in the art.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of known ingredients in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

One of ordinary skill in the art at the time of invention would have been motivated to the particular treatment regimen because the optimization of result effect parameters e.g., dosage range, dosing regimens, dosing duration is obvious as being within the skill of the artisan, involving merely routine skill in the art.

Further, regarding the recitations, "wherein the therapy results in reduction of one or more of incidence of relapse, spasticity and fatigue", "wherein the therapy stabilizes the patients Expanded Disability Status Score, thus halting progress of the disease", in claims 8-9, since Lunardi et al. render the claimed method of administration of effective

amounts of lamotrigine for treating multiple sclerosis obvious, administration of lamotrigine necessarily results in reduction of one or more of incidence of relapse, spasticity and fatigue", halts progress of the disease, as claimed herein.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shobha Kantamneni whose telephone number is 571-272-2930. The examiner can normally be reached on Monday-Friday, 8am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, Ph.D can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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